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Malignant Transformation of Polyostotic Fibrous Dysplasia

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MALIGNANT TRANSFORMATION of fibrous dysplasia of bone has been well documented. Fibrosarcoma, osteosarcoma, chondrosarcoma, and other rarer sarcomas have been described as arising from fibrous dysplasia.[1-3] Previous radiation therapy may or may not be associated with this occurrence.[3-5] We wish to report the evolution of nonirradiated polyostotic fibrous dysplasia into a poorly differentiated sarcoma which at autopsy showed the histologic characteristics of a malignant mesenchymal tumor with features of rhabdomyosarcoma.

CASE REPORT

A 25-year-old white woman in whom a diagnosis of polyostotic fibrous dysplasia was made at 2 years of age developed a tumor of the left hip. She had never received radiation therapy and there was no history of precocious puberty. A hip disarticulation performed eight months before death disclosed a bosselated, 8 x 12 cm, partially encapsulated tumor occupying the neck of the femur. The cut surface of the tumor was focally excavated and light tan-gray to red, and there were several areas of pale nodularity extending down into the medullary portion of the femoral shaft, with similar areas in the medullary portion of the tibia. The final histologic interpretation was polyostotic fibrous dysplasia involving the femur and tibia of the left leg (Fig 1) with fibrosarcomatous degeneration of the major upper femoral lesion (Fig 2). Roentgenograms of the surgical specimen demonstrated the bony lesions (Fig 3).

Rapid recurrence necessitated further resection, but the tumor continued to progress, and radiologic studies revealed bony lesions in the left superior pubic ramus. The patient received actinomycin D and 5,000 rads of local radiation, but three months before death there were pulmonary nodules for which she was treated with vincristine, cyclophosphamide (Cytoxan), and actinomycin D.

On final admission one month before death the patient presented as a cachectic young woman with substernal chest pain and breakdown of the amputation site. There was marked masculinization characterized by a beard and male distribution of body hair. The blood pressure was 110/70 mm Hg, the pulse 120/min, and the temperature 98.6 F (37 C). Laboratory values included hematocrit, 34%; WBC, 16,200/cu mm; BUN, 13 mg/100 ml; alkaline phosphatase, 31.5 IUB (international unit-Bodansky) and SGOT 12.0 IUB. She was treated for wound infection and given supportive care, but her condition deteriorated and she died on the 28th hospital day.

PATHOLOGIC FINDINGS

Gross Findings

At necropsy the scalp hair was extremely thin. Prominent dark facial hair was present over the upper lip and on the chin, and the skin had a mild increase in pigmentation, but without cafe-au-lait spots. An 11 x 4 cm ulceration was present at the amputation site of the left hip.

The lungs contained large metastatic nodules and together weighed 1,545 gm. The cut surface of the tumor was white and fleshy with areas of hemorrhagic necrosis. Tumor extended through the pleura of the left lung and into the left lateral chest wall.

A 10 cm tumor extended into the left pelvic cavity from the posterolateral pelvic wall. Periaortic lymph nodes were extensively replaced and enlarged by tumor, and a solitary 0.6 cm white tumor metastasis was present in the left lobe of the liver. The adrenals together weighed 12 gm and were grossly normal. The ovaries were not grossly involved with the tumor.

Light Microscopy

The tumor was very cellular and was composed of pleomorphic cells, many of which were multinucleated giant cells. The cells generally were ovoid to polyhedral and many strap cells were present (Fig 4). Some of the bizarre, pleomorphic nuclei contained large nucleoli. Although the eosinophilic cytoplasm contained no definite cross striations on H & E or PTAH stains, the overall pattern resembled rhabdomyosarcoma.

Histologically the tumor was essentially similar from all sites sampled except for tissue from a mass in the right lung which resembled a fibrosarcoma, with bundles and bands of smaller, more spindle-shaped anaplastic cells (Fig 5). Trichrome stains of the tumor from all sites revealed no fibrous tissue. No tumor invasion or hyperplastic changes were present in adrenal gland tissue. Ovarian tissue demonstrated only fibrosis and stromal hyperplasia; thin layers of tumor partially rimmed each ovary. Lipid stains on unfixed, frozen ovarian tissue showed lipid deposits in the areas of stromal hyperplasia.

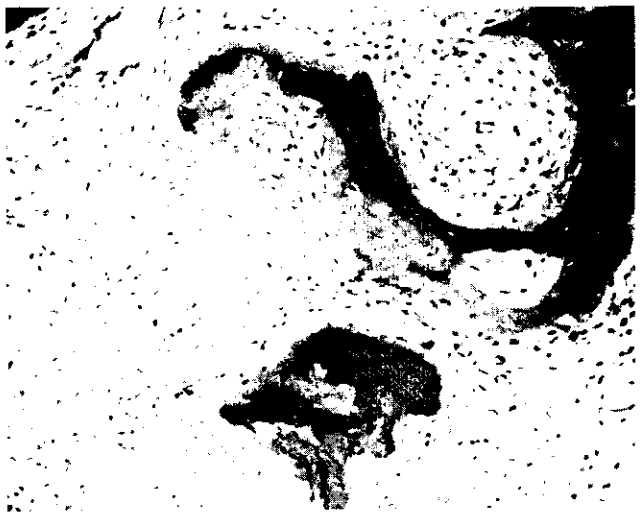

FIGURE 1. Microscopic appearance of fibrous dysplasia involving femoral shaft in surgical amputation. (H & E, original magnification x 100)

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FIGURE 2. Microscopic appearance of femoral malignancy—a poorly differentiated sarcoma resembling fibrosarcoma. (H & E, original magnification x 400)

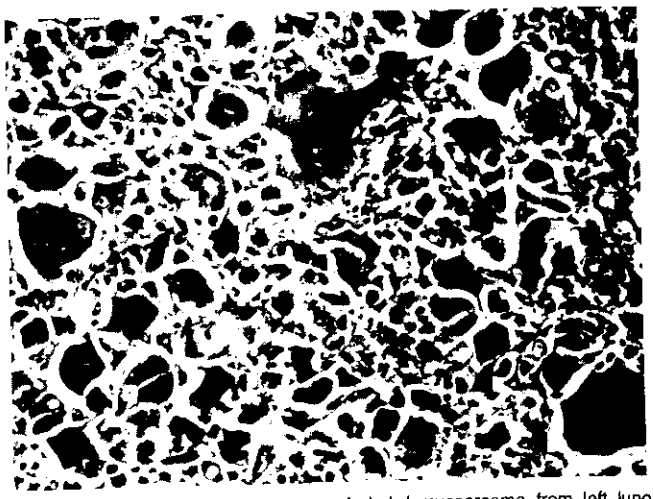

FIGURE 4. Microscopic appearance of rhabdomyosarcoma from left lung metastasis. Pleomorphic cells include spindle, oval, and polygonal shapes. Some cells are elongated and strap-like. Giant cells with bizarre hyperchromatic nuclei are present. (H & E, original magnification x 400)

Electron Microscopy

A portion of the formalin-fixed pelvic tumor was washed several times with phosphate buffer, and after fixation in 2.5% glutaraldehyde and postfixation in osmium tetroxide, was embedded in epon. Thin sections were examined with a Hitachi H-11 electron microscope.

The electron micrographs showed malignant cells containing large pleomorphic nuclei with irregular chromatin. The cytoplasm showed the characteristic myofibrils and Z bands of skeletal muscle cells, confirming the diagnosis of rhabdomyosarcoma (Fig 6).

Special Studies

A determination of the testosterone level on an autopsy serum specimen revealed a value of 143 ng/100 ml. This was compared to control samples from two male subjects whose serum had been drawn at approximately the same interval after death. The values

FIGURE 3. (A) Roentgenogram of femoral head and neck of surgical specimen shows destruction and distortion of bony architecture by tumor. (B) Proximal tibia of surgical specimen shows area of bone destruction characteristic of fibrous dysplasia.

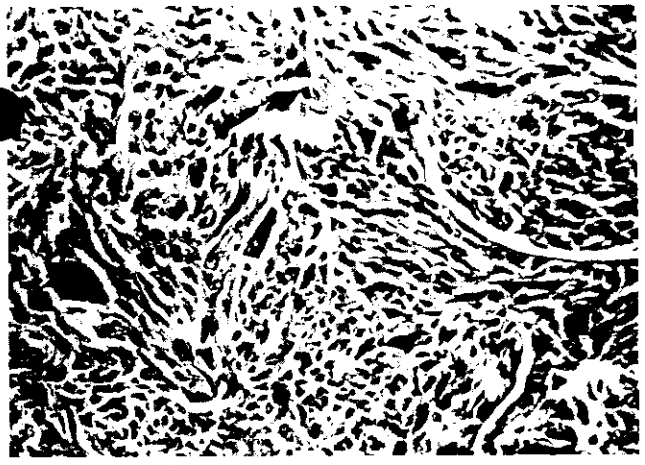

FIGURE 5. Tumor from right lung metastasis. Smaller, more spindle-shaped anaplastic cells are arranged in bundles and bands. Strap-shaped cells and giant cells are also present. (H & E, original magnification x 200)

FIGURE 6. Electron micrograph of tumor cell containing myofibrils and Z bands (arrows), as seen in rhabdomyosarcoma. (Original magnification x 27,000)

obtained were 48 and 110 ng/100 ml, indicating probable adsorption of the testosterone onto blood components, since normal living values for males are in the range of 200 ng/100 ml. The value of 143 ng would therefore seemingly indicate a very high testosterone level in our patient before death, which is consistent with the observed masculinization.

COMMENT

Isolated fibrous dysplasia of bone consists of foci of fibrous replacement of normal bone architecture and may occur in a single bone (monostotic) or in two or more bones (polyostotic). The cause is unknown. No familial or hereditary factors have been recognized. The frequency of occurrence of fibrous dysplasia has been recorded as 2.5% of all bone neoplasms.[6] The craniofacial bones, femur, tibia, and ribs are most commonly affected.[1,3] Albright's syndrome is polyostotic fibrous dysplasia with endocrine abnormalities and cutaneous pigmentation.

Fibrous dysplasia may transform into a variety of mesenchymal malignant tumors, but usually only into neoplasms comprising elements of bone, cartilage, or connective tissue as are present in the lesion.[7] The incidence of malignant change of fibrous dysplasia in the general population is variously reported as 0.4%[3] and not over 10%.[7] The frequency of histologic types of malignant tumors associated with fibrous dysplasia and occurrence in monostotic or polyostotic disease is shown in the Table. More malignancies are reported as arising from polyostotic disease than from monostotic. By far, the most common tumor type is osteogenic sarcoma; less frequently fibrosarcoma, chondrosarcoma, giant and spindle cell tumors, and combinations of these types have been described.

Retrospective study of the tumor histology from the surgical specimen of this case revealed a poorly differentiated mesenchymal tumor resembling a fibrosarcoma. The subsequent differentiation into an apparent rhabdomyosarcoma appears to be unique, and

TABLE. Tumor Histology From Collected Cases in the Literature of Malignant Transformation of Fibrous Dysplasia*

	Osteosarcoma	*Fibrosarcoma*	*Chondrosarcoma*	*Spindle Sarcoma*	*Giant Cell Sarcoma*	*Spindle & Giant Cell Sarcoma*	*Fibrosarcoma & Chondrosarcoma*	*Other*
Schwartz and Alpert[3] 1964	13P 4M	5M	1P 1M	1M	1P			1P 1M
Riddell[2] 1964	1P 1M			1P	1P			
Bell and Hinds[9] 1967		1P						
Slow and Friedman[10] 1971	1P							
Dabska and Buraczewski[7] 1972			1M	1M			1M	
Huvos et al[3] 1972	4P 4M		1M	1M		1P	1P	
Feintuch[4] 1973			1P					
Total	28	6	5	4	2	1	2	2

*The number of cases reported by each author has been adjusted where cases have been reported more than once.
P = Polyostotic
M = Monostotic

the role of therapeutic irradiation on the evolution of the tumor histology must be considered, because it was only after radiation therapy that the tumor assumed the histologic features of rhabdomyosarcoma.

The masculinization observed in this patient is an additional feature of interest. Luteinization of metastatic tumor to the ovary as reported by Scully and Richardson[8] is a possibility. The high plasma testosterone levels may be related to ovarian metastasis and would explain the masculinizing features which this patient exhibited. No abnormalities in adrenal size or histology were identified.

SUMMARY

We have described an unusual case of polyostotic fibrous dysplasia in a 25-year-old white woman who had malignant transformation into a mesenchymal tumor with widespread metastases and features of rhabdomyosarcoma. Masculinization also occurred with high plasma testosterone levels. A mechanism for the development of masculinizing features is discussed.

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Postpartum Thrombophlebitis of the Ovarian Vein

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POSTPARTUM ILEOFEMORAL THROMBOSIS was first described by White in 1784. Blood stasis, physical changes in the vessel wall, and biochemical alterations in blood have come to be considered the main predisposing factors.[1] During pregnancy, the ovarian veins are dilated sixtyfold and the smooth muscle hypertrophy in the media of the vein acts as a protective mechanism to withstand the additional load of pregnancy.[2,3]

Morbidity and mortality from thromboembolism during the puerperium remains a significant problem; it presents during the five days after delivery and is independent of gravity or parity. The most common cause of thromboembolism is phlebitis, usually secondary to streptococcal infection.[4] The first reported pulmonary embolus from bilateral ovarian vein thrombosis was that described by Duff et al.[5]

Ovarian vein thrombophlebitis is a rare but life-threatening complication of puerperium. In pregnancy, the right ovarian vein is the more frequently involved.[6] Deliveries are usually normal and the symptoms may include fever, low abdominal pain, and occasionally mild leukocytosis. An abdominal mass is almost always palpable. The differential diagnosis should include pyelonephritis, acute appendicitis, twisted ovarian cyst, ovarian torsion, pyosalpinx, hematoma of the broad ligament, degenerated fibrinoid, volvulus, perinephric abscess, thrombosis of the pampiniform plexus, and parametritis.[5,6]

Infection, with associated changes in the vein wall, as well as the increased blood coagulability before and after childbirth play a significant role in the right ovarian vein syndrome and other related thromboembolic situations. Treatment consists of ligation or excision of the thrombosed ovarian vein. The inferior vena cava should be ligated if the thrombus extends into the lumen and thrombectomy cannot be done. Heparin is of value in the postoperative period since it prevents clot propagation.[7]

CASE REPORT

A 25-year-old woman (para 0-1-1-0), with a past history of Stein-Leventhal syndrome diagnosed by laparoscopy, began complaining of diffuse abdominal pain two days after normal vaginal delivery of a premature infant. Her pulse rate was 132/min, temperature was 100 F (37.8 C), and she was normotensive; urinalysis and electrolyte values were normal. Blood cultures were negative; chest and abdominal roentgenograms were normal.

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